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Sleep Disorders

RECOGNITION

Recognition of sleep disorders is important because:

- They are common, affecting approximately 10–15% of the US population.
- Many medical, neurological, and psychiatric disorders present with sleep problems.
- Sleep disorders can have a significant affect on a patient's physical, social, and occupational life.

SLEEP: THE BASICS

Non-Rapid Eye Movement Sleep

1. Electroencephalographic features:
   - Stage 1: drowsiness; disappearance of alpha wave, mild slowing of background.
   - Stage 2: light sleep; spindle wave, vertex sharp wave, K-complexes.
   - Stages 3 and 4: deep sleep, slow waves (theta and delta).
2. Decreased body temperature. Increased vagal tone.
3. Normal muscle tone.
4. Increased growth hormone secretion.

Rapid Eye Movement, or Active, Sleep

1. Electroencephalogram features: similar to stage 1 non-rapid eye movement (NREM), presence of rapid jerky eye movements, saw-tooth waves.
2. Decreased muscle tone except for extraocular muscles, diaphragm, and occasional limb jerks.
3. Increased autonomic activities: increased body temperature, increased basal metabolic rate, increased blood pressure, pupillary dilatation, sweating, irregular breathing, increased brain activity, and cerebral blood flow.
4. Penile erection.
5. Dreaming.

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Sleep Cycles

In adults, sleep begins with NREM. The first REM sleep occurs within 70–90 minutes; successive REMs occur every 90 minutes. Four to six REM cycles occur during 7–8 hours of sleep. In adults, REM constitutes about 20% of total sleep. After age 60, there are virtually no stages 3 and 4 of NREM.

Biological Rhythms

Circadian rhythm cycles about every 24 hours, but in most of us, the sleep–awake cycle is about 25 hours (ultradian).

Neuroanatomy

Raphe nuclei in the pons are the source of NREM, and the lateral geniculate nucleus of the pons are the source of REM. Serotonin is the major neurotransmitter for sleep.

SLEEP DISORDERS

Insomnias

Insomnia is a chronic lack of adequate sleep to maintain normal daytime function. Transient insomnia is common. Chronic insomnia could be caused by medical, neurological, psychiatric, and drug/alcohol problems, or it can be idiopathic. Most parasomnias are associated with insomnia. Treatment depends on the underlying cause. Low doses of sedative–hypnotic medications (benzodiazepines) are used for disabling insomnias.

EXCESSIVE DAYTIME SLEEPINESS

Narcolepsy

- Incidence: 1:1000–1:10,000.
- Onset: 20–40 years, equally affects men and women. Not only is the patient at risk for accidents, but there is also significant social affects.
- Highly associated with HLA-DR2, and HLA-DQ1 and HLA-DQB1 proteins.
- Excessive daytime sleepiness: sleep attack, last 10–15 minutes during sedentary situation, often leaves the patient feeling refreshed on awakening.
- Cataplexy: sudden onset of hypotonia after an exciting or emotional event (laugh, anger, etc.), lasting 1–2 minutes. Eye and respiratory muscles are usually spared. Recently, it has been shown that approximately 90% of narcoleptics with cataplexy have no detectable neuropeptide orexin or hypocretin in their cerebral spinal fluid. Orexin-producing neurons are located in the lateral hypothalamus (Orexin-A and -B).

- Sleep paralysis: generalized weakness, during falling asleep or on awakening, lasting a few minutes. Can be frightening.
- Hypnagogic hallucination: vivid (auditory or visual) hallucination during sleep or on awakening.

Diagnosis

Patients suspected of having narcolepsy syndrome should be referred to a sleep center. The diagnostic procedures include an overnight polysomnogram to assess the quality of sleep and rule out other possible associated sleep disorders, followed by a daytime multiple sleep latency test in which the latency of five naps is measured within 2 hours. Latency less than 5 minutes is abnormal. Narcolepsy is highly suggestive if patient had two or more stages of sleep-onset REM during this test. Measuring cerebral spinal fluid orexin (hypocretin) level is useful if cataplexy is present. The assay for this protein is now available in some sleep centers. Measurement of HLA-DQB1 might be considered in selected cases.

Treatment

The goal of treatment in patients presenting with sleep attacks (excessive daytime sleepiness) is to increase alertness during daytime, when the patient has to be awake (work, driving, etc.). Sleep hygiene and avoiding drugs causing insomnia are important.

- **Modafinil.** This agent is probably the drug of choice in men and in women who are not on contraceptives. It is not amphetamine-related. The dose is 200–400 mg, given in morning and mid-day.
- **Amphetamines.** These drugs include dextroamphetamine, methamphetamine, and methylphenidate. Methylphenidate (Ritalin) is commonly prescribed. The dose is 5–20 mg, twice during the daytime. Some patients may require higher doses.
- **Tricyclic antidepressants, clorimpramine, venlaflaxin, fluoxetin.** These compounds are generally used in patients with sleep paralysis and cataplexy.
- **Gamma hydroxybutyrate (Xyrem).** This agent is a metabolite of gamma-aminobutyric acid and is the only Food and Drug Administration-approved drug for treatment of cataplexy, sleep paralysis, and hypnagogic hallucination. The dose is 2–4.5 mg, at bedtime in a divided dose.

Sleep Apnea Syndrome

Sleep apnea syndrome (SAS) is periodic cessation of breathing ($\geq$10) during sleep, with periods of awaking, usually by loud snore. Occasional brief apnea is generally normal. There are three types of SAS: obstructive sleep apnea, central type, and mixed.

Obstructive Sleep Apnea

Obstructive sleep apnea is seen in obese, middle-aged (30–60 years) men and women with short necks. Thoracic movement is intact, but there is no airflow through the nose during sleep.

Symptoms and signs. The symptoms of obstructive sleep apnea are early-morning headache, excessive daytime sleepiness, fatigue, poor concentration, and decreased libido. Loud snoring after an apneic episode is observed by sleep partner. On examination, these individuals are obese, have short necks, and often they have neck collar sizes larger than $17^1/_2$. Enlarged tonsils, adenoids, or micrognathia are seen in some. About half of patients have hypertension, and there are a few with pulmonary hypertension, polycythemia, and cardiac arrhythmias.

Central Sleep Apnea

With central sleep apnea, there is cessation of chest and upper air flow during sleep. Symptoms are similar to those of obstructive sleep apnea. The etiology is unknown.

Mixed Sleep Apnea

Mixed sleep apnea is a combination of both obstructive and central apneas. It probably is more common than the other two.

Complications of SAS

Complications of SAS include cardiac arrhythmia, hypoxia, pulmonary hypertension, night heart failure, hypertension, stroke, polycythemia, and asystole.

Diagnosis

SAS is suspected in patients presenting with excessive daytime sleepiness or early morning headaches who are obese, have short and wide necks, and their bed partners report loud snoring, or apnea or choking during sleep. Many sleep labs do not do overnight polysomnograms, daytime multiple sleep latency tests, or maintenance of wakefulness test, because they are time-consuming and expensive. Other practical and easier tests include the Epworth Sleep Scale, which is an eight-question self-administered test. With this test, most SAS patients score more than 10 points. Some labs now recommend use of portable machines. The Eden-Trace recording system is a four-channel respiratory monitor that can measure respiratory flow and airflow.

Treatment

- Weight loss (which is often difficult to maintain).
- Avoidance of alcohol.

- Diuretic: acetazolamide (Diamox), 1000 mg/day.
- Antidepressants.
- Aminophylline.
- Continuous positive airway pressure or bilevel positive airway pressure. Continuous positive airway pressure is now the treatment of choice. It is important to educate the patient to maintain good compliance.
- Surgeries. Uvulopalatopharyngoplasty is now applied to patients with severe SAS who do not respond to conservative treatment. Other techniques include radiofrequency tissue ablation and tracheostomy. Removal of enlarged tonsils, adenoids, or masses is also helpful.

PARASOMNIAS

Parasomnias are abnormal behavior or physiological events that occur exclusively or are exacerbated during sleep.

NREM Parasomnias

Enuresis (bedwetting). Bedwetting beyond age 5 is abnormal; it occurs primarily during stages 3 and 4. Primary cases are usually because of neurological or maturational lag and often are familial. Secondary cases are because of urological, psychological, or medical (diabetes) problems.

Treatment: low-dose imipramine, tricyclic antidepressants, behavioral therapy.

Sleepwalking. Sleepwalking, or somnambulism, is a complex behavior, characterized by walking, climbing, running, or doing odd thing during stages 3 and 4. Sleepwalking occurs in 10% of adults and is often associated with sleep eating or sleep talking. The patient awakens confused. Usually, the onset is in childhood (17%) and disappears after adolescence. The individuals should be protected from self-injury. Benzodiazepines are given to prevent injury.

Sleep talking (somniloquy). This is a common problem, and many people experience it. It could be associated with sleepwalking.

Teeth-grinding (bruxism).

Night terror (pavor nocturnus). Night, or sleep, terror is characterized by sudden onset of a scream or cry, and is associated with autonomic hyperactivation: tachycardia, tachypnea, and sweating. If awakened, patient is confused and has no recollection of the night terror. Common in childhood, it disappears by adolescence. It could cause serious injury. It occurs in 3% of children and 1% of adults. Mothers should be given assurance that the condition is benign and temporary.

Sleep myoclonus (hypnic jerks). Sudden body jerks during stages 1 and 2. Treatment is low-dose clonazepam (0.5–1 mg) at bedtime.

Periodic limb movements. Stereotyped, rhythmic head or limb movements, seen most frequently in children. Benzodiazepines or antidepressants can be given for treatment.

Posttraumatic stress disorder. Subjective sleep complaints, flashbacks, or nightmares. Any emotional trauma may lead to posttraumatic stress disorder. PTSD is often associated with nightmare.

Restless-leg syndrome (RLS). RLS causes unpleasant, indescribable sensation of legs, resulting in the irresistible urge to move the limbs. RLS occurs as patients are beginning to rest or in transition of awake to sleep. Restless arm syndrome has rarely been reported. It is often associated with nocturnal myoclonus. RLS may be primary, with strong family history or secondary to medical (uremia, diabetes, iron deficiency), neurological (peripheral neuropathy), or psychiatric illnesses. Women are most affected. Peripheral neuropathy and iron deficiency should be ruled out. Iron replacement is recommended for most patients. The drug class of choice is the dopamine agonists: pramipexole (Mirapex) or ropinirole (Requip), starting with a low dose and slow titration. Other drugs include clonazepam, temazepam (Restoril), carbamazepine, Sinemet, and opioids.

REM Sleep Parasomnias

REM Sleep Behavior Disorder

REM sleep behavior disorder (RBD) is a recently described sleep disorder affecting about 0.5% of general population. It affects elderly men and is characterized by nondirected, violent behavior such as kicking, punching, yelling, and running, during REM sleep. Patients with RBD act upon their dream; in these individuals, hypotonia or atonia during REM does not occur. RBD is suspected when the patient or the patient's bed partner complains of injury during sleep. The patient has no control or recollection of the behavior during sleep. RBD is commonly associated with or precedes degenerative diseases of the central nervous system such as Parkinson's disease, Huntington's disease, olivopontocerebellar atrophy, dementias, multisystem atrophy, and spinocerebellar degeneration. The drug of choice is clonazepam, with a starting dose of 0.5–1 mg at night. If the patient does not respond to clonazepam, imipramine, carbamazepine, clonidine, Sinemet, or gabapentin may be tried.

Nightmares

Nightmares are frightening dreams that usually awaken individuals from REM sleep. This condition occurs at any age and may be associated with medical or psychological problems. Nightmares should be differentiated from complex partial seizures. Treatment involves behavioral therapy to correct the

underlying medical illness. Cyproheptadine (Periactin), 4–24 mg, at night, might be helpful.

REM Sleep Sinus Arrest

This condition is sinus cardiac arrest during REM sleep, recently described in the literature. Clinically, these individuals may present with early-morning lightheadedness, blurred vision, or chest pain. The condition could be related to autonomic hyperactivity during REM. With the severe form, the patient may require pacemaker.

Impaired or Painful Penile Erection

Impairment of penile erection or painful erection is a disorder occurring during REM sleep, affecting primarily middle aged men.

SLEEP–WAKE (CIRCADIAN) SLEEP DISORDERS

Jet lag is frequently seen in overseas travelers and best managed by continuation of daylight activities at the destination and trying to sleep according to local time. In severe cases, a trial of melatonin might be helpful (5 mg). Another disease is sleep-phase syndrome (nurses, police officers, i.e., people who do shift work), which often requires no specific treatment.